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TRANSMITTAL LETTER (General - Patent Pending)	Docket No. MSU 4.1-587

In Re Application Of: **Evangelyn C. Alocilja and Zarini Muhammad-Tahir**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/074,499	02/13/2002	Leon Y. Lum	21036	1641	4246

Title: **CONDUCTIMETRIC BIOSENSOR DEVICE, METHOD AND SYSTEM**

COMMISSIONER FOR PATENTS:

Transmitted herewith is:

Reply Brief under 37 C.F.R. 41.41 with respect to the Examiner's Answer mailed on November 4, 2005.

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Dated: **December 15, 2005**

Ian C. McLeod
Registration No. 20,931
McLeod & Moyne, P.C.
2190 Commons Parkway
Okemos, Michigan 48864
(517) 347-4100

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	: 10/074,499	Confirmation No. 4246
Applicants	: Evangelyn C. Alocilja and Zarini Muhammad-Tahir	
Title:	: CONDUCTIMETRIC BIOSENSOR DEVICE, METHOD AND SYSTEM	
Filed	: February 13, 2002	
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REPLY BRIEF UNDER 37 C.F.R. § 41.41

Sir:

This is a Reply brief in response to the Examiner's answer mailed November 04, 2005 in the above entitled application. The claims on appeal are set forth as in the Claims Appendix.

(1) Real Party in Interest

The real party in interest is the Board of Trustees operating Michigan State University, East Lansing, Michigan, a constitutional corporation of the State of Michigan, which is the assignee of the above entitled application.

(2) Related Appeals and Interferences

There are no pending related appeals and interferences.

(3) Status of Claims

Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are pending in the application. Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 were rejected. Claims 4-6, 11-13, 17, 20, 23 and 25 were subject to a restriction requirement and were canceled in the prosecution. No claims have been allowed.

(4) Status of Amendments

An Amendment under 37 C.F.R. 1.116 was mailed on June 08, 2005. The amendment was entered.

(5) Summary of Claimed Subject Matter

The claimed subject matter in Claim 1 is a biosensor device (Support for this Claim is found at page 3, line 16 through page 4, line 6 of the specification; illustrated in Figures 1A-1E) which comprises:

a strip of a substrate (page 10, lines 2-4 of the specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first capture reagent (page 9, lines 4-11 of the specification) bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a

second capture reagent bound to an electrically conductive polymer in absence of electrically conductive metal particles (page 9, line 12 through page 10, line 1 of the specification), wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex (page 10, lines 8-9 of the specification), the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the analyte. The operation of the biosensor device is illustrated in Figures 2A-2C1 as described at page 11, lines 7-18.

The claimed subject matter in Claim 7 is a system for detecting an analyte in a fluid sample (Support for this Claim is found at page 5, line 7 through page 6, line 4 of the specification) which comprises:

(a) a biosensor device which comprises:

a strip of a substrate (page 10, lines 2-4 of the specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first capture reagent (page 9, lines 4-11 of the specification) bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive polymer in absence of electrically conductive metal particles (page 9, line 12 through page 10, line 1 of the specification), wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex (page 10, lines 8-9 of the specification), the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes;

(b) electrical means for supplying an electrical bias between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after

application of the sample in the second zone to detect the analyte (digital multimeter 19 in Figure 6A as described at page 18, lines 23-28; and Figure 4 as described at page 19, line 22 through page 20, line 1). The operation of the biosensor device is illustrated in Figures 2A-2C1 as described at page 11, lines 7-18.

The claimed subject matter in Claim 8 is a biosensor device (Support for this Claim is found at page 6, lines 5-25 of the specification illustrated in Figures 1A-1E) which comprises:

a strip of a substrate (page 10, lines 2-4 of the specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first antibody (capture reagent of page 9, lines 4-11 of the specification) bound to the substrate in a defined area between electrodes on different sides of the defined area (immobilization of antibody on page 17, lines 3-17) for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the

second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer in absence of electrically conductive metal particles (antibody labeling with polyaniline on page 16, lines 11-20; page 9, line 12 through page 10, line 1 of the specification), wherein when a fluid sample containing an antigen enters the second defined area of the second zone, the antigen is bound by the second antibody which is bound to the conductive polymer to form a complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the antigen (analytical procedure on page 18, lines 6-28).

The claimed subject matter in Claim 14 is a system for detecting an antigen in a fluid sample (Support for this Claim is found at page 7, line 25 through page 8, line 22 of the specification illustrated in Figures 1A-1E) which comprises:

(a) a biosensor device which comprises:

a strip of a substrate (page 10, lines 2-4 of the

specification) having at least two zones (page 10, lines 5-7 of the specification) wherein a

(1) first of the zones contains a first antibody (capture reagent of page 9, lines 4-11 of the specification) bound to the substrate in a defined area between electrodes on different sides of the defined area (immobilization of antibody on page 17, lines 3-17) for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer in absence of electrically conductive metal particles (antibody labeling with polyaniline on page 16, lines 11-20; page 9, line 12 through page 10, line 1 of the specification), wherein when a fluid sample containing an antigen enters the second defined area of the second zone, the antigen is bound by the second antibody which is bound to the conductive polymer to form a complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as

measured between the electrodes (analytical procedure on page 18, lines 6-28);

(b) electrical means for supplying an electrical bias between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after application of the sample in the second zone to detect the antigen (digital multimeter 19 in Figure 6A as described at page 18, lines 23-28; and Figure 4 as described at page 19, line 22 through page 20, line 1).

(6) Grounds of Rejection to Be Reviewed on Appeal

(a) Claims 1-2, 7-9, 14-16, 18-19 and 21 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim *et al.* (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Sigal *et al.* (U.S. Patent No. 6,319,670 B1).

(b) Claims 3, 10, 22, 24 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim *et al.* (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Sigal *et al.* (U.S. Patent No. 6,319,670 B1) as applied to Claims 1, 8 and 14, and further in view of Roberts *et al.* (U.S. Patent No. 5,958,791).

(7) Argument

A. The Examiner rejected Claims 1-2, 7-9, 14-16, 18-19 and 21 under 35 U.S.C. §103(a) as being unpatentable over Kim *et al.* (*Biosensors & Bioelectronics* 2000, 14: 907-915) in view of Sigal *et al.* (U.S. Patent No. 6,319,670 B1). In particular, it was stated in the rejection that one of ordinary skill in the art at the time of the invention would have had a "reasonable expectation of success" in substituting the polyaniline microparticles of Sigal *et al.* for the gold bead of Kim *et al.*

To establish a *prima facie* case of obviousness, basic criteria must be met. There must first be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. This teaching or suggestion to make the claimed combination must be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). There is no teaching or suggestion to modify the cited references or combine the reference teachings so as to provide the claimed biosensor

device.

Kim *et al.* discloses a conductimetric membrane strip immunosensor for the detection of human serum albumin (HSA) as an analyte. Kim *et al.* teaches the use of antibodies against the HSA analyte which have been conjugated to colloidal gold particles as a signal generator for the conductimetric immunosensor. Kim *et al.* teaches first to affinity purify antibodies against human serum albumin (HSA) and then to conjugate the affinity purified antibodies with colloidal gold particles. (Kim *et al.* page 908, last paragraph). The colloidal gold-antibody conjugate is added to a site on the glass fiber membrane before adding an aqueous sample containing the HSA analyte. The sample is absorbed by capillary action into a membrane strip system which is illustrated in Figure 1. The colloidal gold-antibody conjugate binds the analyte to form a complex which travels up the strip to a signal generation pad where an immobilized antibody, also against the HSA analyte, binds the analyte in the complex. The colloidal gold particles captured on the signal generation pad result in a colored signal which can be quantified by optical density values. (Kim *et al.* page 910, second column, last paragraph).

As an alternative to this colorimetric method of detection, "the density of particulate gold, electron-rich metal, can be determined by measuring electric conduction." (Kim *et al.*: page 911, section 3.2, first paragraph). Kim *et al.* teaches placement of two electrodes in the region where the immobilized antibodies bind the analyte in the complex. Since the immobilized antibodies bind the analyte in the complex between the two electrodes, electrical conductivity was monitored. Kim *et al.* teaches however, that the conductivity signal is "so weak that the maximum signal-to noise ratio was approximately two times lower than the value determined by the photometry. The dose-response curves further revealed that the monitoring based on conductimetry involved a comparatively large variation." (Kim *et al.*: page 911, right column, second paragraph).

Kim *et al.* teaches that with the plain gold particles, poor analytical performances in generating the conductimetric signal "could result from an impaired transfer of electrons along the gold particles spread on the membrane surface." (Kim *et al.* "Discussion", page 913, first paragraph). After conjugating the gold particles to the antibody the "residual surfaces of the gold particles

were blocked by adding 0.1 M Tris, pH 7.6, containing 5% casein (1 ml) for 30 min." (Kim *et al.* sentence spanning page 908 and page 909). Kim *et al.* adds the casein as a protein blocking layer for reducing non-specific interactions with the gold particles. Kim *et al.* teaches that since the gold particles are surrounded with protein molecules, *i.e.* immunoglobulin and casein as blocking agent for reducing non-specific interactions, an ionic polymer shell is rendered on the outside of the gold. (Kim *et al.* "Discussion", page 913, first paragraph). "This ionic polymer shell may interfere with electron hopping, a dominant process of charge-transfer between the conducting mediators." (Kim *et al.* page 913, first paragraph of right column) Kim *et al.* further states that because "protein molecule could behave similarly to amorphous semiconductor, the shell thickness exceeding the distance required for efficient electron relay acts as a barrier against conduction." Kim *et al.* initially attempted to resolve the conduction barrier problem by using an external blocking molecular layer of polyethylene glycol instead of the casein. However, Kim *et al.* conclude:

> "Under the given conditions, the signal-to-noise ratio was enhanced by 30% as compared with the

> ionic protein coating, however the performance was still inferior to that of colorimetric detection. Therefore, it was concluded that the conductimetric analysis was relatively insensitive and was unsuitable for the system employing the conventional gold colloids as label."

(Kim *et al.*: first paragraph of Discussion, page 913).

Kim *et al.* then takes a different approach in an attempt to resolve the problem due to the electronic barrier surrounding the gold. After combining the antibody solution with the gold particles for conjugation, Kim *et al.* "introduced, on the surface, polymeric conductor molecules that may bridge the neighboring particles or at least bring them closer to improve the charge-transfer state." Kim *et al.* uses polyaniline as the polymeric conductor molecule. "[P]olyaniline solutions diluted with PB in different concentrations (0.01-1 mg/ml) were added into the mixtures of gold and antibody and then reacted for 30 min." Kim *et al.* teaches that "[w]hen the polyaniline solution is added to the gold suspension, the molecules diffuse to the particle surface and subsequently adsorb to form an ordered layer on the residual sites after the antibody coating." (Kim *et al.*: page 913, right column, last paragraph). An illustration of the polyaniline polymer adsorbed on the surface of the gold particles is shown in the top frame of

Figure 4 on page 912.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). The teachings of Kim *et al.* would have suggested to those of ordinary skill in the art to keep the gold particles. In an attempt to resolve the electronic barrier problem, Kim *et al.* did not in any way suggest replacing the gold particles with other conducting particles but rather to introduce polymeric conductor molecules to improve the charge transfer *between* the gold particles. As taught by Kim *et al.* the "protrusion degree of the polymer strands, acting as a wire (*i.e.* molecular wires) for electrical connection, outside from the surface (refer to the top of Fig. 4) mainly depends on the polymer concentration applied and the molecular dimension." (Kim *et al.*: page 913, right column, last paragraph). The "extended filaments of the polymer in a plethora cross-linked the particles." (Kim *et al.*: page 913, right column, last paragraph).

Kim *et al.* makes it clear that the gold particles

are important for the generation of the biosensor signal. One advantage of having the gold particles surfaces as taught Kim *et al.* is that "the presence of polymer strands on the surfaces may result in a high interfacial capacitance and, thus, a gain of conduction." (Kim *et al.*: first full paragraph, page 914). Kim *et al.* teaches that interfacial capacitance due to the presence of polymer strands on the surface of the gold particles is a major contributor to signal generation in a low range of the gold concentration.

> "In a low range of gold concentration, the conductimetric signal increased in approximate proportion to the optical density, which could indicate the interfacial capacitance as a major contribution to the signal generation."

(Kim *et al.*: first full paragraph, page 914). This knowledge would not lead a person of skill in the art to remove the gold particles and directly conjugate the antibody or other capture reagent directly to the polymeric conductor molecules. This teaching of an interfacial capacitance would actually strongly suggest that the gold particles are important components of the system, since the surface of the gold particles can generate an interfacial capacitance which contributes to the signal generation. Additionally, the gold particles are necessary to generate

color which can be detected in addition to the conductivity. (Kim *et al.*: page 910, right column).

It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). Kim *et al.* teach the strategy of using the colloidal gold-antibody conjugates with the conducting polymer and not the direct labeling of the antibody with the conducting polymer by chemical reaction "because, in such a case, the protein molecule itself does not contain available sites for electron relay." (Kim *et al.*: Conclusions, page 914). Therefore, one skilled in the art reading Kim *et al.* would be directed away from eliminating the metal (gold) particles since Kim *et al.* teaches that direct labeling of the antibody with the polymer would not have the electron relay sites on the antibody protein molecule which are necessary for conduction.

It was stated in the rejection that it would have been obvious to substitute the metal bead of Kim *et al.* with the polymer bead of Sigal *et al.* since Sigal *et al.* teach that the materials to make electrically conductive microparticles are interchangeable and suitable for the same

purpose. Sigal *et al.* disclose methods for performing electrochemiluminescence assays using electrically conductive microparticles having a first assay-ligand (such as an antibody) immobilized on it surface. A second assay-ligand (such as an antibody) is immobilized on an electrode surface. The antibodies can each bind an analyte of interest so as to form a complex, thereby binding the electrically conductive complex to the electrode surface. Thus, the conductive microparticles are bound directly to the electrodes. Sigal *et al.* do not teach a biosensor device similar to the claimed invention, therefore Sigal *et al.* would not show or suggest using the polymer bead as a substitute for the gold particles of Kim *et al.* Using the polymer beads of Sigal *et al.* in place of the gold particles of Kim *et al.* does nothing to solve the conductivity problems associated with using the gold beads which Kim *et al.* attempts to resolve. Thus, there is nothing to motivate a person of ordinary skill in the art to use conductive polymer beads to replace the gold particles described by Kim *et al.*

According to MPEP 2144.06, in order to rely on equivalence as a rationale supporting an obviousness

rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958); *In re Scott*, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another.) Even if the polymer beads of Sigal *et al.* were able to perform the same function as the gold particles of Kim *et al.*, using conductive polymer beads is not an obvious modification in view of the gold particles of Kim *et al.* There is no suggestion to make the combination of the device of Kim *et al.* with functionally or mechanically equivalent conductive polymer beads in any of the cited prior art.

There is nothing in the references which would suggest the desirability using conductive polymer beads, since the using conductive polymer beads do nothing to address the problems which are associated with using the

gold particles of Kim *et al.*. Nothing in the cited references would suggest that it would no longer be necessary to block the bead surfaces with protein molecules as a blocking agent for reducing non-specific interactions with the bead. Therefore, an ionic polymer shell would still be rendered on the bead surfaces upon addition of the protein molecules. This ionic polymer shell would still cause a conduction barrier similar to the one described by Kim *et al.* Using polymer beads in place of the gold particles of Kim *et al.* does nothing to solve the conductivity problems associated with using the gold beads. A person of ordinary skill in the art would recognize that replacing the gold particles with a polymer bead does not lead to a solution to the conductivity problem, and therefore the person of skill in the art would have no motivation to modify the references in this manner.

One consideration which applies to obviousness rejections is that the references must be viewed without the benefit of hindsight vision afforded by the claimed invention. "It is difficult but necessary that the decision maker forget what he or she has been taught . . . about the claimed invention and cast the mind back to the time the

invention was made (often as here many years), to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Replacing the gold particles of Kim *et al.* with the conductive polymer beads of Sigal *et al.* in place of the gold particles appears to be an example of using impermissible hindsight reasoning. Nothing in Kim *et al.* would suggest replacing the gold particles with a conductive polymer bead. Sigal *et al.* teach completely unrelated electrochemiluminescence assays using microparticles and as such adds nothing to motivate a person of skill in the art to make the combination in the claimed biosensor device. Therefore, the cited references when viewed as a whole do not suggest the desirability and thus the obviousness of making this combination.

B. The Examiner rejected Claims 3, 10, 22, 24 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim *et al.* (Biosensors & Bioelectronics 2000, 14: 907-915) in view of Sigal *et al.* (U.S. Patent No. 6,319,670 B1), and further in view of Roberts *et al.* (U.S. Patent No. 5,958,791).

Claims 3, 10, 22, 24 and 26 are patentable over Kim *et al.* and Sigal *et al.* for the reasons discussed above. Additionally, with regards to Claims 22, 24 and 26, Kim *et al.* and Sigal *et al.* further fail to teach a multiple array of devices so that multiple analytes are detected simultaneously from the same sample. Roberts *et al.* teaches test devices including multiple sets of interdigitated electrode arrays for simultaneous multiple analyte detection and assay of a test sample for a plurality of analytes. However, Roberts *et al.* does not teach a *single* multiple array as taught by Applicants as illustrated in Figure 3. The simultaneous multiple analyte detection taught by Roberts *et al.* uses multiple sets of interdigitated electrode arrays in order to perform simultaneous multiple analyte detection to assay the test sample for a plurality of analytes. The liposome-enhanced immunoassay and test

device taught by Roberts *et al.* would not suggest to a person of ordinary skill in the art the single multiple array as taught by Applicants, since the nature of the immunoassay and test device taught by Roberts *et al.* requires separate competitive binding portions 104 and measurement portions 106. The test of Roberts *et al.* requires that a test mixture with the analyte of interest first passes through a competitive binding portion 104 having the binding material for the analyte before passing through a liposome lysing portion 106 where a liposome lysing agent releases the electroactive marker from the liposome. The electroactive marker is then carried by the migrating mixtures, via capillary action, into and through the electrochemical measurement portion to complete the electrical circuit (Roberts *et al.*: col. 15, line 53 through col. 16, line 5). A *single* multiple array as taught by Applicants and illustrated in Figure 3, wherein a plurality of analytes in a mixture can each be individually detected at one of the multiple regions 21A to 21D would not be suggested by the cited prior art references. In the embodiment illustrated in Figure 3, each one of the analytes bind to a specific capture reagent/antibody at one of the

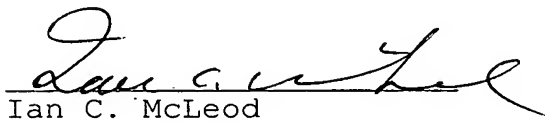
zones between the electrodes to generate a signal at one of the regions 21A-21E representative of that particular analyte. Each analyte will generate one of an array of simultaneous voltage signals 33 which is proportional to the change of the resistance in that region. The immunoassay and test device taught by Roberts *et al.* does not show or suggest such an array, since specific binding must be completed *before* the test mixture flows between the electrodes in the measurement portion 106. If the adjacent electrodes are spaced too closely together in the immunoassay and test device taught by Roberts *et al.*, the electroactive marker can diffuse over to an adjacent region to generate a false signal in that region. Due to this possibility, the electrode arrays of Roberts *et al.*, unlike those arrays taught by Applicants, must be maintained at a large enough distance so that no electroactive markers can diffuse over the electrodes in an adjacent measurement portion 106. The design of the device taught by Applicants does not have this problem with cross over signal. Since only the first capture reagent specific for the desired analyte is present between the electrodes only the desired complex of the analyte and second capture reagent bound to

the electrically conductive polymer will be bound between the electrodes. Therefore any signal measured across the electrodes of any of the regions 21A to 21D is generated by specific binding of the desired analyte to the region.

C. Conclusion

As shown above, the device and system of the present invention is not obvious over the cited prior art references. Therefore, Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are each patentable. Reversal of the Final Rejection is requested.

Respectfully,



Ian C. McLeod
Registration No. 20,931

McLEOD & MOYNE, P.C.
2190 Commons Parkway
Okemos, MI 48864

Telephone: (517) 347-4100
Facsimile: (517) 347-4103

CLAIMS APPENDIX

(As noted in Examiner's Answer, amendments to Claims 1, 7, 8 and 14 made in the Amendment Under 37 C.F.R. §1.116 mailed on June 08, 2005 were inadvertently left out of the Claims Appendix in the Appeal Brief. The following claims incorporate the changes.)

1. A biosensor device which comprises:

a strip of a substrate having at least two zones wherein a

(1) first of the zones contains a first capture reagent bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive polymer in absence of electrically conductive metal particles, wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex, the complex migrates to the first zone in the medium and the

analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the analyte.

2. The device of Claim 1 wherein the device further comprises a third zone adjacent to the first zone into which the fluid is absorbed after passing through the first defined area of the first zone.

3. The device of any one of Claims 1 or 2 wherein the first defined area has a dimension between the electrodes of 1.0 mm or less.

7. A system for detecting an analyte in a fluid sample which comprises:

(a) a biosensor device which comprises:

a strip of a substrate having at least two zones wherein a

(1) first of the zones contains a first capture reagent bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive polymer in absence of electrically conductive metal particles, wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex, the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes;

(b) electrical means for supplying an electrical bias between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after application of the sample in the second zone to detect the analyte.

8. A biosensor device which comprises:

a strip of a substrate having at least two zones wherein a

(1) first of the zones contains a first antibody bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer in absence of electrically conductive metal particles, wherein when a fluid sample containing an antigen enters the second defined area of the second zone, the antigen is bound by the second antibody which is bound to the conductive polymer to form a complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the antigen.

9. The device of Claim 8 wherein the device further comprises a third zone adjacent to the first zone into which the fluid is absorbed after passing through the first defined area of the first zone.

10. The device of any one of Claims 8 or 9 wherein the first defined area has a dimension between the electrodes of 1.0 mm or less.

14. A system for detecting an antigen in a fluid sample which comprises:

(a) a biosensor device which comprises:

a strip of a substrate having at least two zones wherein a

(1) first of the zones contains a first antibody bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and

(2) a second of the zones containing a fluid transfer

medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second antibody bound to an electrically conductive polymer in absence of electrically conductive metal particles, wherein when a fluid sample containing an antigen enters the second defined area of the second zone, the antigen is bound by the second antibody which is bound to the conductive polymer to form a complex, the complex migrates to the first zone in the medium and the antigen is bound by the first antibody thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes;

(b) electrical means for supplying an electrical bias between the electrodes; and

(c) measuring means for determining a change in the conductivity or resistance of the first area before and after application of the sample in the second zone to detect the antigen.

15. The system of Claim 14 wherein the device further comprises a third zone adjacent to the first zone into which the fluid is absorbed after passing through the first defined area of the first zone.

16. The device of Claim 1 or 2 wherein a third zone adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

18. The system of Claim 7 or 8 wherein a pad adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

19. The device of Claim 8 or 9 wherein a pad adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

21. The system of Claim 14 or 15 wherein a pad adjacent to the second zone is provided for applying the fluid sample containing the analyte prior to being introduced into the second zone.

22. The device of Claim 1 or 2 as a multiple array of devices grouped together separately on the substrate so that multiple analytes can be detected simultaneously from the same sample.

24. The device of Claim 8 or 9 as a multiple array of devices grouped together separately on the substrate so that multiple analytes are detected simultaneously from the same sample.

26. The system of Claim 14 or 15 as a multiple array of devices grouped together separately on the substrate so that multiple analytes can be detected simultaneously from the sample.